JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Interventions to Prevent Perinatal Depression
Evidence Report and Systematic Review for the US Preventive Services Task Force

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IMPORTANCE Depression during pregnancy and the postpartum period is relatively common and can have adverse effects on both mother and child.

OBJECTIVE To systematically review benefits and harms of primary care–relevant interventions to prevent perinatal depression, a major or minor depressive episode during pregnancy or up to 1 year after childbirth, to inform the US Preventive Services Task Force.

DATA SOURCES MEDLINE, PubMED (for publisher-supplied records only), PsycINFO, and the Cochrane Central Register of Controlled Trials; surveillance through December 5, 2018.

STUDY SELECTION Randomized clinical trials (RCTs) and nonrandomized controlled intervention studies of interventions (eg, behavior-based, antidepressants, dietary supplements) to prevent perinatal depression in general populations of pregnant and postpartum individuals or in those at increased risk of perinatal depression. Large cohort studies were considered for harms of antidepressant use only.

DATA EXTRACTION AND SYNTHESIS Two investigators independently reviewed abstracts and full-text articles and quality rated included studies. Random-effects meta-analysis was used to estimate the benefits of the interventions.

MAIN OUTCOMES AND MEASURES Depression status; depression symptoms; maternal, infant, and child health outcomes.

RESULTS Fifty studies (N = 22 385) that met inclusion criteria were identified. Counseling interventions were the most widely studied interventions. Compared with controls, counseling interventions were associated with a lower likelihood of onset of perinatal depression (pooled risk ratio [RR], 0.61 [95% CI, 0.47-0.78]; 17 RCTs [n = 3094]; I^2 = 39.0%). The absolute difference in the risk of perinatal depression ranged from 1.3% greater reduction in the control group to 31.8% greater reduction in the intervention group. Health system interventions showed a benefit in 3 studies (n = 5321) and had a pooled effect size similar to that of the counseling interventions, but the pooled effect was not statistically significant using a method appropriate for pooling a small number of studies (restricted maximum likelihood RR, 0.58 [95% CI, 0.22-1.53]; n = 4738; I^2 = 66.3%; absolute risk reduction range, −3.1% to −13.1%). None of the behavior-based interventions reported on harms directly. A smaller percentage of participants prescribed sertraline had a depression recurrence compared with those prescribed placebo (7% vs 50%, P = .04) at 20 weeks postpartum in 1 very small RCT (n = 22 analyzed) but with an increased risk of adverse effects to the mother.

CONCLUSIONS AND RELEVANCE Counseling interventions can be effective in preventing perinatal depression, although most evidence was limited to women at increased risk for perinatal depression. A variety of other intervention approaches provided some evidence of effectiveness but lacked a robust evidence base and need further research.

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Perinatal depression is a common condition that was estimated in 2012 to affect more than 180 000 new mothers (11.5%) annually in the United States and that can have a devastating effect on the mother as well as the infant.[1] Perinatal depression is defined as the occurrence of a major or minor depressive episode during pregnancy or up to 1 year after childbirth.[2] In addition to the typical symptoms of depressive disorders (eg, feeling hopeless, loss of interest in activities that used to be enjoyed, withdrawing from friends and family), other symptoms in the perinatal period may include persistent doubt of the ability to take care of the infant, trouble bonding with the infant, and thoughts of self-harm or harm of the infant.[3]

Risk factors that can be used to identify individuals at risk for perinatal depression include a history of depression,[4-7] history of physical or sexual abuse,[5] unplanned or unwanted pregnancy,[8] stressful life events,[1,5,9] intimate partner violence,[10,11] and complications during pregnancy.[12] Additionally, low socioeconomic status, lack of social support, and bearing children during adolescence have been associated with a greater risk of developing perinatal depression after delivery.[5,6,8,13] Numerous interventions have been proposed to prevent perinatal depression; however, there is no commonly agreed-on method of prevention. Thus, there is likely substantial variation in clinical practice. Although there are risk factors for perinatal depression and interventions exist that may help prevent perinatal depression, the effectiveness of these interventions and the subpopulations who could most benefit need further evaluation.

There are currently no clinical guidelines on how to prevent perinatal depression and no prior US Preventive Services Task Force (USPSTF) recommendation on this topic. This systematic review was conducted to synthesize the evidence related to the effectiveness of interventions in preventing perinatal depression to support a new USPSTF recommendation.

Methods

Scope of Review

The USPSTF commissioned this review to evaluate direct evidence from trials and large cohort studies (for harms of antidepressant use only) on interventions to reduce the risk of perinatal depression initiated during pregnancy or the first year postpartum. Specifically, the 2 key questions (KQs) (**Figure 1**) aimed to identify the benefits (KQ1) and harms (KQ2) of interventions to prevent perinatal depression for pregnant or postpartum individuals and their children. Additional methodological details regarding the review search strategies, detailed study inclusion criteria, quality assessment, excluded studies, and description of data analyses are publicly available in the full evidence report at http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/perinatal-depression-preventive-interventions.

Data Sources and Searches

Comprehensive literature searches were performed for primary literature in MEDLINE, PubMed (for publisher-supplied records only), PsycINFO, and the Cochrane Collaboration Registry of Controlled Trials from January 2012 through February 6, 2018. Database searches were supplemented with suggestions from preidentified experts in the field and by reviewing reference lists from other relevant systematic reviews. After February 2018, ongoing surveillance continued through article alerts and targeted searches of high-impact journals to identify major studies published in the interim that could affect the conclusions or understanding of the evidence and affect the related USPSTF recommendation. The last surveillance was conducted on December 5, 2018, and resulted in the addition of no new studies.

Study Selection

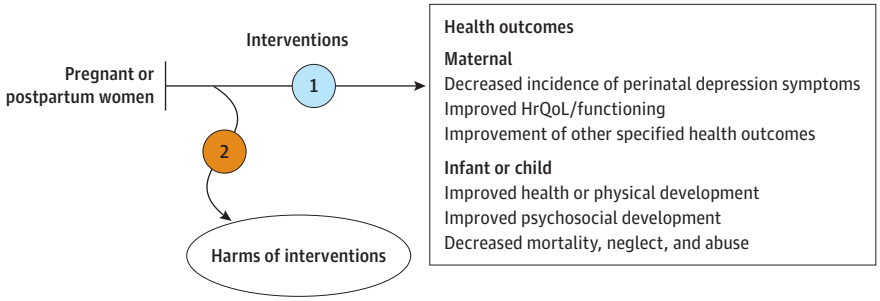
Two reviewers independently reviewed abstracts and full-text articles against specified inclusion criteria (**Figure 2**). Studies were eligible if they were published in English, conducted in countries ranked as having "very high" human development according to the World Health Organization, and included pregnant persons or mothers up to a maximum of 1 year postpartum. Studies limited to persons with mental health symptoms or disorders (eg, anxiety disorders) were eligible; however, studies limited to perinatal individuals currently experiencing or being treated for a depressive episode were excluded, as were studies limited to persons with psychotic or developmental disorders. In addition, studies limited to persons with a medical condition (eg, HIV/AIDS), and those limited to persons in institutions (eg, psychiatric inpatients) or long-term care or residential facilities were excluded because of generalizability concerns. Studies that included a subset of these types of participants were included; however, it was required that the number not exceed 50% of the total sample to be considered for inclusion.

Studies were required have a primary or secondary aim to prevent perinatal depression. The following interventions were included: counseling (eg, cognitive-behavioral therapy [CBT], interpersonal therapy [IPT]), psychoeducation, or other supportive interventions (eg, peer mentoring); care delivery models targeting improved mental health outcomes; prophylactic use of antidepressants; widely available physical activity or complementary and alternative therapies; and hormonal therapy. Pharmacotherapy harms were only to be evaluated for medications that were found to support the prevention of perinatal depression and were to be examined only during the phase (pregnancy or postpartum) in which the evidence was identified. Interventions composed of general parenting education without a mental health component (eg, prenatal or infant care classes) were excluded.

Depression diagnosis (determined through a clinical interview) or symptoms (measured using a validated instrument) were a required outcome for included studies. Other maternal health outcomes, infant and child outcomes, birth outcomes, and any information reported on harms were also abstracted. Relevant outcomes reported at least 6 weeks after the baseline assessment or intervention initiation were included, although harms outcomes reported any time after the intervention was initiated were considered.

Interventions that were conducted in or recruited from primary care or a health care system, or that could potentially be implemented in or referred from primary care, were included. This included interventions taking place in primary care clinics; prenatal clinics; obstetrics/gynecology clinics; pediatric clinics; family planning clinics; military health clinics; school-based health clinics; mental health clinics; and research settings, homes, or other community settings, including electronic or computer-based interventions. Studies conducted in correctional facilities, school classrooms, worksites, and emergency departments were excluded.

Figure 1. Analytic Framework: Interventions to Prevent Perinatal Depression



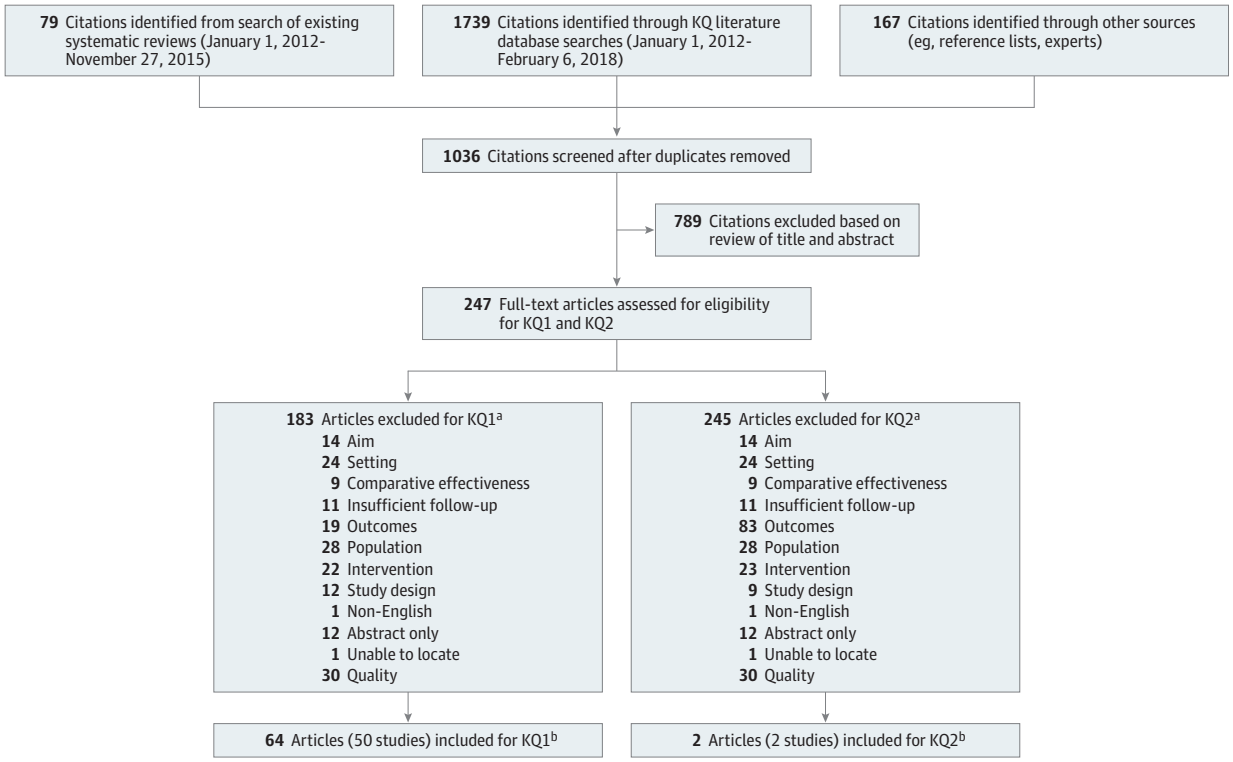
Key questions

1 Do interventions to prevent perinatal depression improve health outcomes in pregnant or postpartum women or their children?
a. In trials that limit enrollment to high-risk women, how are participants identified as being at high risk of developing perinatal depression?

2 What harms are associated with interventions to prevent perinatal depression in pregnant or postpartum women?

Evidence reviews for the US Preventive Services Task Force (USPSTF) use an analytic framework to visually display the key questions that the review will address to allow the USPSTF to evaluate the effectiveness and safety of a preventive service. The questions are depicted by linkages that relate interventions and outcomes. Refer to the USPSTF Procedure Manual for interpretation of the analytic framework.[14] HrQoL indicates health-related quality of life.

Figure 2. Literature Search Flow Diagram: Interventions to Prevent Perinatal Depression



KQ indicates key question.

[a] Reasons for exclusion: Aim: Study aim was not relevant. Setting: Study was not conducted in a country relevant to US practice, or not conducted in, recruited from, or feasible for primary care or a health system. Comparative effectiveness: Active comparator (eg, liquid-based cytology vs conventional cytology alone). Outcomes: Study did not have relevant outcomes or had incomplete outcomes. Population: Study was not conducted in an included population. Intervention: Intervention was out of scope. Design: Study did not use an included design. Language: Publication not in English. Quality: Study was poor quality. Unable to locate: Review staff was unable to locate article.

[b] Studies may appear in more than 1 KQ.

Data Extraction and Quality Assessment

Two reviewers applied USPSTF design-specific criteria[14] to assess the methodological quality of all eligible studies. Each study was assigned a quality rating of "good," "fair," or "poor." Discordant quality ratings were resolved by discussion or by a third reviewer and adjudicated as needed. Studies were rated as poor quality

and excluded if there was a major flaw such as very high attrition (generally >40%), differential attrition between intervention groups (generally >20%); substantial lack of baseline comparability between groups without adjustment; or major concerns about the trial conduct, analysis, or reporting of results. One investigator extracted study-level data using data entry forms developed in DistillerSR (Evidence Partners) and a second investigator confirmed the accuracy of the data.

Data Synthesis and Analysis

Summary tables showing study, population, intervention characteristics, and outcomes were created. Studies were examined overall and grouped according to intervention type: counseling, health system, physical activity, education (without counseling, extensive skills practice, or other supportive interventions), support (without counseling or skill-building), infant sleep, debriefing (exploring the events and emotions of the birth experience, with a counselor providing normalization and education), other behavior-based approaches, antidepressants, and supplements. The intervention categories were developed post hoc, and some trials were difficult to categorize and could possibly have fit into more than 1 category. The one that appeared to have the best fit was chosen by the primary investigator.

Because of its clinical utility, depression status was chosen as the primary outcome. Most trials reported a related dichotomous depression outcome: cumulative incidence of depression, prevalence, or the proportion scoring above a cutoff on a symptom severity scale. Since most trials excluded women with depression or high symptom levels at baseline, it was assumed that most cases of depression identified after the start of the study would be new-onset cases, but not necessarily first-onset cases, since many women had previous episodes of depression.

Strength of evidence was rated for each key question, based on consistency (similarity of effect direction and size), precision (degree of certainty around an estimate), reporting bias (potential for bias related to publication, selective outcome reporting, or selective analysis reporting), and study quality (ie, study limitations).

Random-effects models on both the main outcome of depression status and continuous measures of depression symptom severity were conducted, both overall and separately by intervention. The DerSimonian and Laird model for pooling was used, and I^2 and Q statistic were calculated to test for heterogeneity. In addition, because the DerSimonian and Laird method is prone to insufficient coverage of the full 95% confidence intervals when the number of studies is small and statistical heterogeneity is high, restricted maximum likelihood models with the Knapp-Hartung correction for small samples were used when fewer than 10 trials were pooled and the DerSimonian and Laird model showed a statistically significant effect. For the full body of evidence, a funnel plot was generated and the Egger test was performed to explore small-study effects, which can be related to publication bias.[15] Additionally, meta-regression and sensitivity analyses were conducted to explore factors associated with effect size for the dichotomous depression status outcome.

Stata version 15.1 (StataCorp LP) was used for all analyses. All significance testing was 2-sided, and results were considered statistically significant if the *P* value was .05 or less.

Results

Two reviewers independently assessed 1036 abstracts and reviewed 247 full-text articles. In total, 50 studies (8 good quality, 42 fair quality; N = 22 385; 49 randomized clinical trials [RCTs][16-64] and 1 nonrandomized controlled intervention study[65]) were included (Figure 2; eTable 1 in the Supplement). Of the 50 included studies, 20 (40%) were conducted in the United States, and most recruited women from primary care or obstetrics/gynecology practices (33/50 [66%]) or from other clinical settings (13/50 [26%]) such as in the hospital postdelivery, through electronic medical records, or in clinic- or hospital-based childbirth education classes (**Table 1**; eTable 2 in the Supplement). Twenty-six of the included studies (52%) recruited pregnant women, 22 (44%) recruited postpartum women, and 2 (4%) recruited women who were pregnant as well as those up to 26 weeks postpartum.[16,17] Most studies (42/50 [84%]) were limited to women 18 years or older, but 1 was limited to adolescents[18] and 7 had no age restrictions.[19-25] The studies assessed the effect of a wide range of intervention approaches, including counseling, health system–level interventions, physical activity, supportive interventions, education, infant sleep advice, birth-experience postpartum debriefing, expressive writing, yoga, omega-3 fatty acids, sertraline, and nortriptyline. For all KQs, additional descriptive and outcome data are available in the full report.

Twenty-seven studies (54%) selected women at increased risk for perinatal depression, such as having a personal or family history of depression (or perinatal depression), elevated depressive symptoms, or socioeconomic (eg, low income, single, young, recent intimate partner violence) or mental health (eg, elevated anxiety symptoms) risk factors (Table 1). The most common approach was to select women on the basis of depression symptoms or history.[16,17,26-35] The Edinburgh Postnatal Depression Scale (EPDS; range, 0-30; higher score indicates greater distress) and the Center for Epidemiologic Studies Depression Scale (CES-D; range, 0-60; higher score indicates greater distress) were the most widely used tools for identifying women at risk for developing postpartum depression in the included studies.

Although the majority of participants in the included studies were non-Hispanic white (69% of all participants in trials that reported race/ethnicity), 2 trials were limited to Latina women,[27,28] and 8 had majority black and Latina samples.[16-18,36-40] In addition, 13 studies (26%) were primarily or entirely composed of economically disadvantaged women.[16,17,22,27,28,37-44]

Benefits of Preventive Interventions

Key Question 1. Do interventions to prevent perinatal depression improve health outcomes in pregnant or postpartum women or their children?

Key Question 1a. In trials that limit enrollment to high-risk women, how are participants identified as being at high risk of developing perinatal depression?

Counseling Interventions

Twenty RCTs (2 good quality, 18 fair quality) of counseling interventions were identified (n = 4107). Seventeen of these reported incidence, prevalence, and exceeding symptom cutoff and are

Table 1. Summary of Study Characteristics, by Intervention Type

Intervention Category	No. of Studies (No. of Participants)	No. of Studies (%)									
		Good Quality	Conducted in the United States	Intervention Group Initiated During Pregnancy	Adults Only	Screening or Outreach[a]	Population Selection Depression Only	Population Unselected	Excluded Depression Diagnosis/High Symptoms[b]	Majority Nonwhite	Primarily Low-SES Participants
Overall	50 (22 385)	8 (16)	20 (40)	26 (52)	42 (84)	42 (84)	12 (24)	23 (46)	20 (40)	11 (22)	13 (26)
Counseling	20 (4107)	2 (10)	12 (60)	17 (85)	17 (85)	17 (85)	6 (30)	5 (25)	13 (65)	8 (40)	10 (50)
Health system	3 (5321)	0	0	1 (33.3)	2 (66.7)	3 (100)	0	3 (100)	1 (33.3)	0	0
Physical activity	3 (1200)	1 (33.3)	0	2 (66.7)	3 (100)	3 (100)	0	3 (100)	0	0	0
Education	6 (2949)	2 (33.3)	2 (33.3)	2 (33.3)	5 (83.3)	6 (100)	1 (16.7)	5 (83.3)	1 (16.7)	2 (33.3)	1 (16.7)
Support	7 (4569)	2 (28.6)	0	2 (28.6)	5 (71.4)	7 (100)	2 (28.6)	3 (42.9)	2 (28.6)	0	2 (28.6)
Sleep	3 (980)	0	1 (33.3)	0	3 (100)	2 (66.7)	0	1 (33.3)	0	1 (33.3)	0
Debriefing	2 (2786)	0	0	0	1 (50)	2 (100)	0	1 (50)	0	0	0
Expressive writing	1 (120)	0	0	0	1 (100)	1 (100)	0	1 (100)	0	0	0
Yoga	1 (46)	0	1 (100)	1 (100)	1 (100)	0	0	0	0	0	0
Antidepressants	2 (80)	0	2 (100)	0	2 (100)	1 (50)	2 (100)	0	2 (100)	0	0
Omega-3 fatty acids	2 (227)	1 (50)	2 (100)	1 (50)	2 (100)	0	1 (50)	1 (50)	1 (50)	0	0

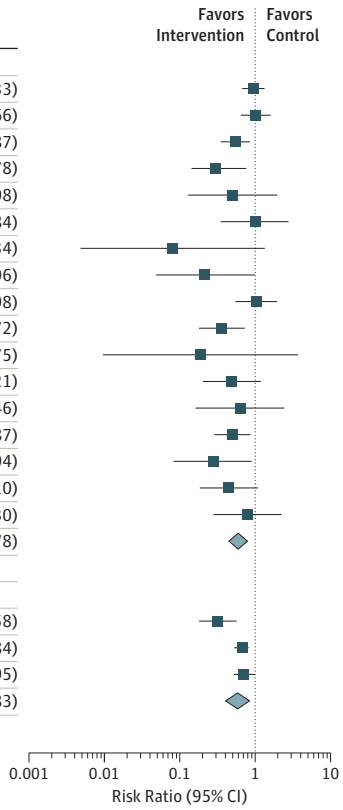
Abbreviation: SES, socioeconomic status.

[a] Number recruited via screening or outreach vs volunteer opt-in.

[b] Studies excluded persons with a diagnosis of depressive disorder or who met an a priori threshold for symptoms of depression (eg, exceeded a specified score on a screening test).

Figure 3. Depression Incidence, Prevalence, or Exceeding a Symptom Cutoff for Counseling and Health System Interventions, Sorted by Follow-up Time

Source	Intervention	Planned Follow-up, wk[a]	Outcome	No. With Depression/Total (%)		Risk Ratio (95% CI)
				Intervention	Control	
Counseling						
Kozinszky et al,[50] 2012	CBT, IPT	p06	LQ ≥12	54/609 (8.9)	77/829 (9.3)	0.95 (0.69-1.33)
Leung and Lam,[48] 2012	IPT	p06	EPDS >12	25/78 (32.1)	24/78 (30.8)	1.04 (0.66-1.66)
Ortiz Collado et al,[42] 2014[b]	Tourne	p09	EPDS ≥12	24/92 (34.3)	27/58 (45.5)	0.56 (0.36-0.87)
Milgrom et al,[47] 2011	CBT	p12	BDI-II ≥14	6/47 (12.8)	16/42 (38.1)	0.34 (0.14-0.78)
Brugha et al,[19] 2000	CBT	p13	Prevalence	3/94 (3.0)	6/96 (6.0)	0.51 (0.13-1.98)
Zlotnik et al,[39] 2011	IPT	p13	Incidence	6/25 (24.0)	5/21 (23.8)	1.01 (0.36-2.84)
Zlotnik et al,[37] 2001	IPT	p13	Incidence	0/17 (0)	6/18 (33.0)	0.08 (0.00-1.34)
Zlotnik et al,[38] 2006	IPT	p13	Incidence	2/46 (4.3)	8/40 (20.0)	0.22 (0.05-0.96)
Cooper et al,[49] 2015	NR	p18	Prevalence	16/80 (20.0)	15/79 (19.0)	1.05 (0.56-1.98)
Dimidjian et al,[29] 2016	CBT, MT	p26	Incidence	8/43 (18.4)	22/43 (50.2)	0.36 (0.18-0.72)
Muñoz et al,[28] 2007	CBT	p26	Prevalence	0/21 (0)	2/20 (10.0)	0.19 (0.01-3.75)
Phipps et al,[18] 2013	IPT	p26	Incidence	6/48 (12.5)	13/52 (25.0)	0.50 (0.21-1.21)
Gorman,[21] 1997	IPT	p26	Prevalence	3/20 (15.0)	4/17 (23.5)	0.64 (0.17-2.46)
Zlotnik et al,[40] 2016	IPT	p26	Incidence	16/101 (16.0)	30/96 (31.0)	0.51 (0.30-0.87)
Tandon et al,[17] 2011	CBT	p32	Incidence	3/32 (9.4)	9/27 (33.3)	0.28 (0.08-0.94)
Tandon et al,[16] 2014	CBT	p40	Incidence	6/41 (14.6)	11/34 (32.4)	0.45 (0.19-1.10)
Le et al,[27] 2011	CBT	p52	Incidence	6/77 (7.8)	7/73 (9.6)	0.81 (0.29-2.30)
Subtotal						0.61 (0.47-0.78)
I^2 = 39.0%; χ^2 test for heterogeneity, P = .051						
Health system						
Fontein-Kuipers et al,[65] 2016	Prenatal	g37	EPDS ≥10	14/218 (6.4)	42/215 (19.5)	0.33 (0.19-0.58)
MacArthur et al,[23] 2002	Postpartum	p17	EPDS ≥13	156/1087 (14.4)	208/977 (21.3)	0.68 (0.55-0.84)
Brugha et al,[51] 2011	Home visitor	p26	EPDS ≥12	113/1474 (7.7)	83/767 (10.8)	0.71 (0.53-0.95)
Subtotal						0.60 (0.43-0.83)
I^2 = 66.3%; χ^2 test for heterogeneity, P = .051						



Weights are from random-effects analysis. BDI-II indicates Beck Depression Inventory II; CBT, cognitive-behavioral therapy; EPDS, Edinburgh Postnatal Depression Scale; IPT, interpersonal therapy; LQ, Leverton Questionnaire; MT, motivational therapy; NR, not reported; RR, risk ratio.

[a] "g" indicates during gestation and "p" indicates postpartum; thus, for example, g37 indicates 37 weeks' gestation and p12 indicates 12 weeks postpartum.

[b] Study-reported adjusted analysis was not statistically significant, although effect size shown in the forest plot, based on unadjusted data, is statistically significant. Tourne indicates a psychosomatic humanist group intervention developed by Dr Claude-Emile Tourne.

included in this pooled estimate; the 3 studies[43,45,46] that did not report these dichotomous measures all reported continuous measures of depressive symptoms, with mixed findings. The pooled risk ratio (RR) for counseling interventions was 0.61 when the outcomes of incidence, prevalence, and exceeding symptom cutoff were combined (95% CI, 0.47 to 0.78; 17 trials [n = 3094]; I^2 = 39.0%) (**Figure 3**). The proportion of participants with depression according to any of the dichotomous depression outcomes at the main time point of 26 weeks postpartum (or the closest to this time point) ranged from 0% to 34% in the intervention groups, compared with 6% to 50% in the control groups, with absolute risk differences (ARDs) ranging from 1.3% greater reduction in the control group to 31.8% greater reduction in the intervention group. Of these 17 trials, 13 (76%) reported an outcome of major depressive disorder diagnosis based on a clinical interview. Trials reported depression outcomes over a wide range of follow-up time points, ranging from 6 to 52 weeks postpartum.

Effects were largest for CBT- and IPT-based interventions (**Table 2**), and the 2 most commonly used approaches were the CBT-based Mothers and Babies program (used in 4 studies[16,17,27,28]) and the IPT-based Reach Out, Stand Strong, Essentials for New Mothers (ROSE) program (used in 5 studies[18,37-40]). The Mothers and Babies program involved 8 to 17 group sessions during pregnancy and postpartum, with a goal of helping participants create a healthy physical, social, and psychological environment for themselves and their infants. The ROSE program involved 4 to 6 sessions during pregnancy and postpartum, covering topics such as stress management, development of a social support system, role transitions and changes associated with role transitions, and types of interpersonal conflicts common around childbirth.

When limited to trials that only included women at increased risk of perinatal depression, the pooled RR was 0.55 (95% CI, 0.44 to 0.68; 14 trials [n = 1411]; I^2 = 0%) (Table 2). There was a statistically significant small-studies effect for the counseling trials (Egger test, −1.52; P = .01). Smaller trials were more likely to limit inclusion to populations selected for increased risk of perinatal depression, which may have been a major source of the association between effect size and study size.

Overall, counseling interventions were associated with a small beneficial effect in symptom score measures, amounting to a pooled

Table 2. Summary of Pooled Effects of Subgroup Analyses for Counseling Interventions, Organized by Counseling Approach

Counseling Approach	No. of Studies (No. of Participants)	Pooled RR (95% CI)	I^2, %	τ^2
All counseling trials	17 (3094)	0.61 (0.47-0.78)	39	0.09
CBT	8 (2128)	0.51 (0.33-0.79)	49	0.17
CBT Moms and Babies Program	4 (325)	0.47 (0.26-0.84)	0	0.0
IPT	8 (2095)	0.71 (0.50-1.00)	42	0.09
IPT ROSE program	5 (464)	0.50 (0.32-0.80)	12	0.04
All counseling trials, limited to trials targeting women at increased risk of perinatal depression	14 (1411)	0.55 (0.44-0.68)	0	0.0

Abbreviations: CBT, cognitive-behavioral therapy; IPT, interpersonal therapy; ROSE, Reach Out, Stand Strong, Essentials for New Mothers; RR, risk ratio.

standardized effect size of 0.2, which would generally be considered a small effect,[66] or a 1.5-point greater reduction in depression symptom severity than control conditions (standardized mean difference, −0.21 [95% CI, −0.40 to −0.02]; 13 trials [n = 1367]; I^2 = 57.2%) [eFigure 1 in the Supplement]; weighted mean difference in change between groups, −1.51 [95% CI, −2.84 to −0.18]; 13 trials [n = 1367]; I^2 = 61.3% [eFigure 2 in the Supplement]). This analysis combined a variety of instruments with 30- to 63-point ranges. Thirteen trials reported continuous symptom score measures and showed a wide range of results; however, group differences were statistically significant in only 5 trials.[16,17,29,37,42]

Most of the counseling trials also reported other maternal or child outcomes; however, there was a wide variety of outcome measures and little consistency across studies. Stress and anxiety were the most commonly reported other maternal or child outcome. For example, 4 trials[42,46-48] reported a measure of stress, but most did not show statistically or clinically important differences between groups. Other outcomes, generally reported by only 1 or 2 studies, included measures of functioning (general,[19,38] maternal,[21] and family[21,42,48]), quality of life,[48] social support,[16,42] trauma symptoms,[39] mental health treatment,[40] breastfeeding,[38] child development,[49] child attachment,[49] birth weight,[42] and preterm birth.[42] Of these, 1 trial (n = 184) showed statistically significant benefits on birth weight (between-group difference, 283 g; P = .01) and incidence of preterm birth (RR, 0.19 [95% CI, 0.06 to 0.65]).[42] No other outcomes were statistically significant.

Fifteen of the 20 trials of counseling interventions (75%) were limited to women who were known to be at increased risk of perinatal depression, owing to depression history or symptoms (6/20 [30%]), non–depression-related risk factors (3/20 [15%]), or either depression-related or other risk factors (6/20 [30%]). Thirteen of the 20 trials (65%) excluded women who met diagnostic criteria for current major depression or scored above a prespecified cutoff on a symptom severity scale. The trials that did not exclude women with a depression diagnosis or high symptom level used either unselected populations or selected participants based on non–depression-related criteria, so the proportion with depression was estimated or reported to be well below 50%.

Counseling interventions lasted a median of 8 weeks (range, 4-70 weeks), included a median of 8 sessions (range, 4-20 sessions), and had an estimated median of 12 hours of contact (range, 4-23.3 hours). Fifteen (75%) included group sessions, 11 (55%) included individual sessions, and 3 intervened with couples (eTable 2 in the Supplement).[19,45,50] Most of the interventions used CBT or IPT approaches. Information on adherence for counseling and other intervention approaches is available in the full evidence report.

Health System Interventions

Three fair-quality studies (n = 5321; 2 RCTs,[23,51] 1 nonrandomized controlled intervention study[65]) examined the effects of health system–level interventions. All 3 programs showed beneficial effects on depression, with RRs ranging from 0.33 (95% CI, 0.19 to 0.58; n = 433; ARD, −13.1%) to 0.71 (95% CI, 0.53 to 0.95; n = 2241; ARD, −3.1%) for exceeding a specified depression symptom level at follow-up. The pooled RR for health system interventions was 0.60 (95% CI, 0.43 to 0.83; 3 studies [n = 4738]; I^2 = 66.3%) (Figure 3). However, this association was not statistically significant with the restricted maximum likelihood analysis, which better accounts for the small number of studies pooled (RR, 0.58 [95% CI, 0.22 to 1.53]). None were conducted in the United States, so applicability to this country may be limited. Additionally, none limited their sample to women at increased risk of depression, suggesting that some universal prevention programs may be effective.

Health outcomes were sparsely reported in these studies and showed mixed results (see full evidence report for more details). No infant or child outcomes were reported in these trials.

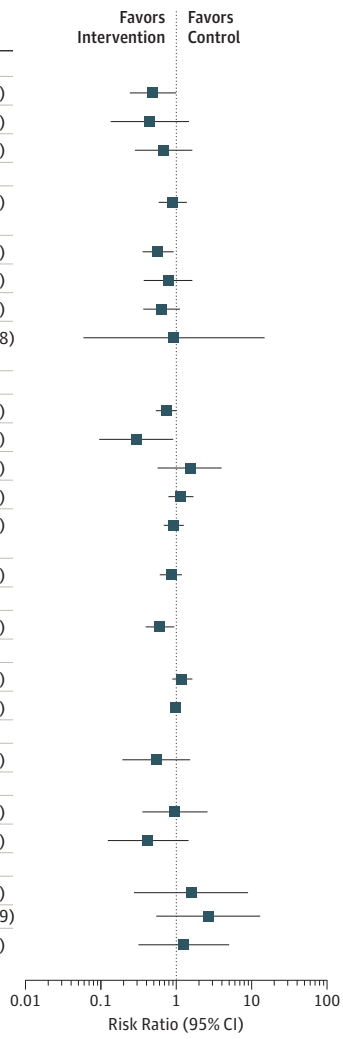
Other Intervention Approaches

A wide variety of other intervention approaches were identified. Some of these approaches showed benefit in some trials, but most trials did not find statistically significant group differences (**Figure 4**, for studies reporting sufficient data to plot). The intervention focus of these studies included physical activity (3 RCTs [n = 1200]),[52-54] education (without counseling or extensive support; 6 RCTs [n = 2949]),[20,30,41,55-57] supportive interventions (without formal counseling; 7 RCTs [n = 4569]),[22,24,31,44,58,59] infant sleep advice (3 RCTs [n = 980]),[36,60,61] birth-experience postpartum debriefing (2 RCTs [n = 2786]),[25,62] expressive writing (1 RCT [n = 120]),[63] antidepressants (2 RCTs [n = 80]),[33,34] supplements (2 RCTs [n = 227]),[35,64] and yoga (1 RCT [n = 46]).[26]

Of these approaches, the physical activity interventions consistently reported point estimates in the direction of benefit (ARDs ranged from −1.3% to −12.5%), but only 1 trial found statistically significant group differences.[53] Birth-experience debriefing[25,62] and omega-3 fatty acid supplementation[35,64] showed no benefit (study RRs ranged from 0.99 [95% CI, 0.87 to 1.11] [n = 1745] to 2.70 [95% CI, 0.56 to 13.09] [n = 79]). Additional sensitivity and subgroup

Figure 4. Depression Incidence, Prevalence, or Exceeding a Symptom Cutoff for Other Intervention Approaches, Sorted by Follow-up Time

Source	Intervention Subtype	Planned Follow-up, wk[a]	Outcome	No. With Depression/Total (%)		Risk Ratio (95% CI)
				Intervention	Control	
Physical activity						
Perales et al,[53] 2015		g39	CES-D ≥16	11/90 (12.2)	19/77 (24.7)	0.49 (0.25-0.97)
Songøygard et al,[54] 2012		p13	EPDS ≥13	4/379 (1.1)	8/340 (2.4)	0.45 (0.14-1.48)
Norman et al,[52] 2010		p16	EPDS >13	7/62 (11.0)	12/73 (16.0)	0.69 (0.29-1.64)
Education						
Maimburg and Vaeth,[57] 2015	Prenatal PPD module	p06	EPDS ≥12	39/543 (7.2)	42/526 (8.0)	0.90 (0.59-1.37)
Heh and Fu,[30] 2003	PPD booklet	p13	EPDS ≥10	14/35 (40.0)	24/35 (68.6)	0.58 (0.37-0.93)
Howell et al,[56] 2014	PPD education	p13	EPDS ≥10	12/235 (5.1)	15/232 (6.5)	0.79 (0.38-1.65)
Howell et al,[41] 2012	PPD education	p26	EPDS ≥10	19/214 (8.9)	29/209 (13.7)	0.64 (0.37-1.10)
Fisher et al,[20] 2016	Postpartum general education	p26	Prevalence	1/185 (0.5)	1/173 (0.6)	0.94 (0.06-14.88)
Support						
Kenyon et al,[22] 2016[b]	Case management	p08	EPDS ≥13	61/489 (12.0)	87/519 (17.0)	0.74 (0.55-1.01)
Dennis,[31] 2003	Peer support	p18	EPDS >12	3/20 (15.0)	11/22 (52.4)	0.30 (0.10-0.92)
Stamp et al,[59] 1995	Support group	p26	EPDS >12	9/60 (15.0)	6/61 (9.8)	1.52 (0.58-4.02)
Reid et al,[58] 2002	Support group	p26	EPDS ≥12	49/339 (14.5)	46/370 (12.4)	1.16 (0.80-1.69)
Wiggins et al,[44] 2004	Community referral	p61	EPDS ≥12	43/155 (27.7)	90/303 (29.7)	0.93 (0.69-1.27)
	Home visitor	p61	EPDS ≥12	38/149 (25.5)	90/303 (29.7)	0.86 (0.62-1.19)
Sleep						
Hiscock et al,[60] 2014		p26	EPDS >9	31/392 (7.9)	51/395 (12.9)	0.61 (0.40-0.94)
Debriefing						
Small et al,[25] 2000		p26	EPDS ≥13	81/467 (17.3)	65/450 (14.4)	1.20 (0.89-1.62)
Priest et al,[62] 2003		p52	Incidence	NR (17.8)	NR (18.2)	0.99 (0.87-1.11)
Expressive writing						
Blasio et al,[63] 2015		p13	BDI-II 13-28	5/57 (8.8)	9/56 (16.0)	0.55 (0.20-1.53)
Antidepressants						
Wisner et al,[33] 2001	Nortriptyline	p17	Incidence	6/26 (23.1)	6/25 (24.0)	0.96 (0.36-2.59)
Wisner et al,[34] 2004[b]	Sertraline	p20	Incidence	3/14 (21.4)	4/8 (50.0)	0.43 (0.13-1.45)
Supplements						
Mozurkewich et al,[35] 2013	EPA-rich fish oil	p06	Incidence	3/39 (7.7)	2/41 (4.9)	1.58 (0.28-8.94)
	DHA-rich fish oil	p06	Incidence	5/38 (13.2)	2/41 (4.9)	2.70 (0.56-13.09)
Llorente et al,[64] 2003	DHA supplementation	p78	Incidence	4/23 (17.4)	3/22 (13.6)	1.28 (0.32-5.06)



Weights are from random-effects analysis. BDI-II indicates Beck Depression Inventory II; CES-D, Center for Epidemiologic Studies Depression Scale; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; EPDS, Edinburgh Postnatal Depression Scale; NR, not reported; PA, physical activity; PPD, postpartum depression; RR, risk ratio.

[a] "g" indicates during gestation and "p" indicates postpartum; thus, for example, g37 indicates 37 weeks' gestation and p12 indicates 12 weeks postpartum.

[b] Study-reported adjusted analyses were statistically significant, although effect size shown in the forest plot, based on unadjusted data, are not statistically significant.

analyses exploring effect sizes by study and intervention characteristics are available in the full report.

The 2 trials of antidepressants to prevent perinatal depression assessed the effects of nortriptyline (n = 58)[33] and sertraline (n = 22).[34] Both trials were conducted in the United States. The trial of nortriptyline found that the drug offered no preventive benefits compared with placebo (Figure 4).[33] Neither the rates of recurrence between participants taking nortriptyline and those taking placebo (23% vs 24%; between-group statistics not reported; $P > .99$), nor the time to postpartum recurrence (detailed findings not reported; exact log-rank ≤0.00; $P = .83$) differed between the 2 groups. The trial of sertraline found that a smaller percentage of participants taking sertraline had a depression recurrence compared with those taking placebo (7% vs 50%; difference in recurrence rates, 0.43 [95% exact CI, −0.01 to 0.84]; $P = .04$) at 20 weeks postpartum.[34] Further, the time to recurrence was faster in those receiving placebo (hazard ratio, 0.11 [95% exact CI, 0.02 to 1.02]; exact Wilcoxon-Gehan $P = .02$). In these trials, women with a history of postpartum depression in the previous 5 years were randomized to receive either an antidepressant (nortriptyline [75 mg/d][33] or sertraline [50 mg/d][34]) or placebo for 17 weeks, starting as soon as possible after birth, followed by a 3-week tapering phase. Neither trial of antidepressants reported other maternal health outcomes or child outcomes.

Harms of Preventive Interventions

Key Question 2. What harms are associated with interventions to prevent perinatal depression in pregnant or postpartum women?

None of the nonpharmaceutical studies reported any global harms outcomes for either mothers or infants. Across all of these

studies, none of the outcomes reported showed any pattern of increased risk of harms, based on group means.

Both antidepressant trials systematically collected adverse event information. In the nortriptyline trial (n = 58),[33] the authors stated that participants tolerated nortriptyline well, reporting no differences in withdrawals attributable to adverse effects, with only 1 person withdrawing from each group. They reported only the number of events for 1 of the 11 adverse effects collected; constipation differed between groups (78% of the women taking nortriptyline vs 22% taking placebo). In the sertraline trial (n = 22),[34] participants receiving sertraline were more likely than those receiving placebo to report dizziness (57% vs 13%, $P = .05$) and drowsiness (100% vs 50%, $P = .02$) but did not differ in rates of other adverse events (but data were not shown). Three women stopped taking sertraline because of adverse effects (21%), compared with none in the control group; however, this difference was not statistically significant. One participant taking nortriptyline and 1 taking sertraline converted to mania or hypomania, while no women taking a placebo did so; this difference was not statistically significant for either agent, although the studies were not powered for this outcome. There were no additional studies that addressed harms of sertraline in postpartum women. Additional harms studies of nortriptyline were not searched for because efficacy was not demonstrated for this treatment in the included studies.

No harms were associated with omega-3 fatty acids, although reports of adverse events were collected spontaneously rather than systematically through a validated instrument and adherence was by self-report. No significant differences in the proportion of participants reporting gastrointestinal adverse effects or adherence with the recommended intervention were reported.

Discussion

The summary of evidence is reported in **Table 3**. This review found that counseling-based interventions, in particular depression-focused CBT and IPT, may be effective in preventing perinatal depression. This evidence was primarily limited to women at increased risk for perinatal depression, such as having current depressive symptoms, a history of depression, low socioeconomic status, and lack of support. The pooled RR of 0.61 for perinatal depression at up to 6 months postpartum for counseling interventions corresponds to a number needed to treat of 13.5 (95% CI, 9.9 to 23.9), assuming a 19% baseline risk of developing perinatal depression. Three different health system–level interventions were also effective in health care settings outside the United States, suggesting that similar interventions developed in US-based health care systems may have the potential to be effective and were not limited to women at increased risk of perinatal depression. In all 3 cases, usual care included home visitation, which may be a valuable intervention, suggesting the potential for even greater benefit compared with usual care in the United States. Additionally, other intervention approaches, such as physical activity or educational approaches, reported some positive findings but lacked robust evidence bases.

Only 2 studies of prophylactic use of antidepressants were identified, showing mixed results. Antidepressants can be an important tool for treatment of depression but have been associated with a number of rare but serious adverse events, including suicidality (in young adults), hyponatremia, seizures, gastrointestinal tract bleeding, and serotonin syndrome.[67,68] The decision to use antidepressants in pregnant persons is complicated and is addressed by only a limited amount of evidence. The use of second-generation antidepressants during pregnancy has been associated with a small but increased risk of a number of serious pregnancy and neonatal outcomes.[69] However, the clinical significance of these increased risks is unclear[70] and most guidelines recommend antidepressants for severe depression, with a preference for sertraline,[71] especially for those breastfeeding.[72]

The findings of this review are similar to those reported in other similarly scoped reviews. A 2013 review on psychosocial and psychological interventions to prevent perinatal depression found that women who received a psychosocial intervention were 22% less likely to develop perinatal depression, compared with usual care (pooled RR, 0.78 [95% CI, 0.66 to 0.93]; 20 studies [n = 14 727]).[73] Another review of interventions designed to prevent perinatal depression found a pooled odds ratio of 0.67 for depressive episodes by 6 months postpartum, after excluding outliers (95% CI, 0.52 to 0.85; 26 studies; $I^2 = 46\%$).[74] That review found no study or intervention characteristic that showed a statistically significant association with effect size.

An ideal method for determining which interventions would benefit persons with varying risk profiles is lacking, but the most common approach in the included trials was to include women with a history of depression or current depressive symptoms as measured by instruments such as the EPDS or CES-D. One study investigating the accuracy of the EPDS to predict future perinatal depression found that a cutoff of 9 or higher at 3 to 5 days postpartum had 82% sensitivity, 95% specificity, and a 43% positive predictive value for a diagnosis of major or minor depression at 8 weeks postpartum.[75] The literature on predicting future perinatal depression includes a variety of patient- and clinician-administered tools, but results have been modest in many cases and need to be replicated.

There were a number of limitations in the studies underlying this review. There were relatively few good-quality trials, and approximately one-third of the trials within the scope of this review were excluded because of their poor quality. Many of these appeared to be pilot studies not designed to provide data on effectiveness of the intervention or that used intervention approaches that proved infeasible or ineffective and so were abandoned in the form studied. Some of these studies, however, could have provided useful information had they been conducted and reported in such a way that they met USPSTF quality standards.

The health system–level interventions in this review had limited applicability to health systems in the United States, especially since they involved enhancing home-visiting services, which are not routinely available in the United States. However, some home-visiting services are available in the United States, and these interventions also included other elements that would be relevant to US-based settings. Interventions designed for implementation in health care systems could involve clinician training, electronic medical records–based tools, and facilitated access to behavioral health specialists embedded in the primary care settings.

Another limitation of the evidence was the small number of trials examining several potentially valuable interventions, such as physical activity, infant sleep education, in-hospital perinatal

Table 3. Summary of Evidence by Key Question and Intervention Type

Intervention	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
KQ1: Benefits of Interventions to Prevent Perinatal Depression						
Counseling	20 (4107)	Counseling interventions reduced the risk of perinatal depression, primarily using cognitive behavioral therapy and interpersonal therapy In pooled analyses, the likelihood of perinatal depression was 39% lower in intervention than control participants (pooled RR, 0.61 [95% CI, 0.47 to 0.78]; 17 trials [n = 3094]; I^2 = 39%) Depression symptom severity was reduced by 1.5 points more in intervention than control participants (WMD, −1.51 [95% CI, −2.84 to −0.18]; 13 trials [n = 1367]; I^2 = 61%; T^2 = 2.9)	Reasonably consistent, reasonably precise	Small studies effect suggests possible overestimate of effect size, many small trials, only 2 good-quality trials Dichotomous depression outcomes are a mix of incidence, prevalence, and being above a severity cutoff	Moderate	60% conducted in the United States, most targeting women at increased risk of PND, most initiating the intervention during pregnancy Interventions are not widely available and require specialized training.
Health system	3 (5321)	All 3 health system interventions reduced the risk of perinatal depression by 29% to 69%, although the pooled effect was not statically significant (REML RR, 0.58 [95% CI, 0.22 to 1.53]; 3 studies [n = 4738]; I^2 = 66.3%) One study each reported improvements in anxiety and SF-36 mental health component scores, but the third found no difference in SF-36 scores	Reasonably consistent, imprecise	One study reported results only for the subset of women who had not developed elevated symptoms by 6 weeks postpartum; no good-quality studies One study was a nonrandomized controlled intervention study	Low	Problematic: all conducted outside the United States in health care systems very different from the United States (eg, postpartum home visitors are part of usual care)
Physical activity	3 (1200)	One of the physical activity trials demonstrated a statistical significant reduction in the risk of perinatal depression, with 12.2% of intervention participants exceeding an EPDS threshold vs 24.7% of control participants Absolute risk differences were smaller and not statistically significant in the other trials	Reasonably consistent, imprecise	Small body of evidence; only 1 study showed statistically significant between-group differences	Insufficient	None conducted in the United States, only included unselected populations; however, studies included both pregnant and postpartum women
Education	6 (2949)	Most trials did not find a benefit; however, 1 of the 2 US-based trials found a promising short-term benefit of a brief PND education session in the hospital after delivery, with 1 brief follow-up telephone call (6.3% of intervention participants had EPDS scores ≥10, vs 11.4% of controls; adjusted OR, 0.45 [95% CI, 0.21 to 0.92]) Effect size was smaller and not statistically significant on replication	Inconsistent, imprecise	Wide variety of approaches, minimal replication or similar interventions; the 1 replicated intervention had mixed findings	Insufficient	Only 2 trials of the same intervention were conducted in the United States
Supportive interventions	7 (4569)	Three trials showed benefits of treatment, although effects were either not large, of marginal statistical significance, or based on a very small sample Telehone-based support by trained peers with history of PND showed most promise	Inconsistent, imprecise	Wide variety of approaches with minimal replication; adherence was very low in 1 of 2 nondirective support group interventions	Insufficient	None conducted in the United States, some embedded in health care systems with very low applicability to the United States
Sleep	3 (980)	Mixed results, but some promising findings, including a 43% reduction in the odds of PND in 1 study (adjusted OR, 0.57 [95% CI, 0.34 to 0.94])	Inconsistent, imprecise	Few studies, no good-quality studies	Insufficient	Only 1 small trial conducted in the United States (n = 54); targeted both early and later postpartum phases

(continued)

Table 3. Summary of Evidence by Key Question and Intervention Type (continued)

Intervention	No. of Studies (No. of Observations)	Summary of Findings	Consistency and Precision	Other Limitations	Strength of Evidence	Applicability
Yoga	1 (46)	No statistically significant or potentially clinically important differences between groups in depression severity (mean difference in change in depression symptoms at posttest, 0.1 [95% CI, −3.2 to 3.5]) or anxiety	Consistency NA, imprecise	Single small fair-quality study	Insufficient	Conducted in the United States, among women with elevated anxiety and depressive symptoms
Debriefing	2 (2786)	No benefit of debriefing the birth experience (pooled RR, 1.04 [95% CI, 0.88 to 1.22]; 2 trials [n = 2662]; I^2 = 27%)	Reasonably consistent, reasonably precise	Only 2 fair-quality trials	Low	Neither conducted in the United States
Expressive writing	1 (120)	Expressive writing not clearly associated with PND risk in single relatively small study (RR, 0.55 [95% CI, 0.20 to 1.53])	Consistency NA, imprecise	Single fair-quality small study	Insufficient	Not conducted in the United States
Antidepressants	Sertraline: 1 (22) Nortriptyline: 1 (58)	Sertraline may reduce the risk of PND, but nortriptyline is unlikely to reduce the risk of PND	Consistency NA, imprecise	Single very small fair-quality study for each agent	Insufficient	Conducted in the United States; recruitment through health care setting, women with a history of PND
Omega-3 fatty acids	2 (227)	Supplementation with omega-3 fatty acids (DHA, EPA) is not associated with a reduced likelihood of PND (pooled RR, 1.71 [95% CI, 0.70 to 4.17]; 2 trials [n = 204]; I^2 = 0%)	Reasonably consistent, reasonably precise	Only 2 trials (1 good quality)	Low	Both US-based, unselected and at-risk populations, including pregnant and postpartum women
KQ2: Harms of Interventions to Prevent Perinatal Depression						
Behavior-based	0	Adverse events were not reported in behavior-based trials, but other outcomes consistently trended in direction of benefit or no effect	Consistency NA, imprecise	No studies directly reported on harms	Low	
Omega-3 fatty acids	1 (126)	No adverse events were reported in either treatment group	Consistency NA, imprecise		Low (DHA)	
Nortriptyline	1 (58)	Nortriptyline was associated with constipation (78% vs 22%), but there were no differences in withdrawal because of adverse effects; 1 patient taking nortriptyline converted to mania (vs none taking placebo)	Consistency NA, imprecise	Underpowered to detect serious adverse events such as conversion to mania	Insufficient	Conducted in the United States
Sertraline	1 (22)	Sertraline with associated with an increased risk of dizziness (57% vs 13%) and drowsiness (100% vs 50%); 3 patients taking sertraline withdrew because of adverse effect (vs none taking placebo); 1 patient taking sertraline converted to mania (vs none taking placebo)	Consistency NA, imprecise	Underpowered to detect serious adverse events such as conversion to mania	Insufficient	Conducted in the United States

Abbreviations: DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; EPDS, Edinburgh Postnatal Depression Scale; KQ, key question; NA, not applicable; OR, odds ratio; PND, perinatal depression; REML, restricted maximum likelihood model; RR, risk ratio; SES, socioeconomic status; SF-36, 36-Item Short Form Health Survey; WMD, weighted mean difference.

depression education with follow-up, and peer counseling. In addition, larger-scale effectiveness trials of CBT and IPT approaches are needed to explore the degree to which these interventions can be scaled up, as well as their applicability to lower-risk, more general primary care populations. More research is also needed on the use of antidepressants and dietary supplements in the role of preventing perinatal depression.

Another important deficit in the literature is a lack of good information on the best way to identify individuals at risk for perinatal depression. Measures of depression symptoms, such as the EPDS, likely provide the most direct association with future perinatal depression. However, evidence is lacking on whether and how to incorporate other risk factors, as well as on who is most likely to benefit from preventive interventions and how those individuals are best identified.

Limitations

The review has several limitations. First, it was challenging to determine whether prevention of perinatal depression was truly an a priori aim; it is possible that some studies were missed that had depression as a specific aim, and some studies may have been included that added the depression prevention aim post hoc after determining that their intervention was effective in preventing depression. Second, both the overall body of evidence and the counseling intervention trials had statistically significant small-studies effects. Smaller trials also tended to use interventions that more directly addressed depression and to offer more intensive interventions, so the small-studies effect may be influenced by these and other study characteristics. However, it could not be determined to what extent the effect might be biasing results and overestimating the effect sizes.

Conclusions

Counseling-based interventions can be effective in preventing perinatal depression, although most evidence was limited to women at increased risk for perinatal depression. A variety of other intervention approaches provided some evidence of effectiveness but lacked a robust evidence base and need further research.

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Author Contributions: Dr O'Connor had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: O'Connor, Senger, Coppola, Gaynes.
Acquisition, analysis, or interpretation of data: O'Connor, Henninger, Coppola, Gaynes.
Drafting of the manuscript: O'Connor, Senger, Coppola, Gaynes.
Critical revision of the manuscript for important intellectual content: Henninger, Gaynes.
Statistical analysis: O'Connor, Gaynes.
Obtained funding: O'Connor, Gaynes.
Administrative, technical, or material support: Senger, Henninger, Coppola.

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